LETTER

Serum Sialic Acid in South Indian Type 2 Diabetic Patients with Microvascular Complications

It is reported that serum sialic acid (SSA) is increased in Type 2 diabetes mellitus and shows a correlation to the presence of micro-[1–3] and macrovascular complications.[4] Pickup *et al*.[5] reported in a pilot study that Asian diabetic patients had higher SSA levels compared to Caucasians matched for age, sex, body mass, and duration of diabetes. There are no reports from patients in India. We therefore measured SSA concentrations in Indian Type 2 patients with different degrees of albuminuria and also with and without retinopathy. One hundred and eight patients (M:F 69 : 39) aged 55 ± 9.8 years with duration of known diabetes 14 ± 6.2 years were studied. Twenty-three, healthy non-diabetic controls of similar mean age and BMI were also tested. Albumin excretion was measured in early morning sample by a qualititative albumin test (TCA turbidity). Albumin/creatinine ratio was measured (A/C ratio normal $<30\ \mu g\ mg^{-1}$ creatinine) in subects without proteinuria. Urine albumin was measured by immunoturbidimetry on a Hitachi 704 (Boehringer Mannheim, Germany). Fasting blood samples were tested for sialic acid, urea, creatinine, HbA_1, serum cholesterol, and triglycerides. SSA was estimated using an enzymatic kit (Boehringer Mannheim, Germany). The procedure employs a coupled enzyme assay reaction involving neuraminidase, N-acetyl neuraminic acid aldolase and pyruvate oxidase. H_2O_2 is formed and estimated by a perioxidase dye system. Between batch variation was less than 7 %. A/C ratio of 30 to 300 $\mu\ mg^{-1}$ was considered as microalbuminuria. Clinical proteinuria was defined as the presence of proteinuria of $\geq 500\ mg\ day^{-1}$ in 24 h urine collection. Blood pressure measurement and opthalmoscopic tests for retinopathy were also done for all study subjects.

Using an upper cut-off value of 2.63 mmol l^{-1} for normal (mean ± SD in the normal controls), only 46 out of the 108 (42.6 %) of the diabetic patients had high values of SSA. Diabetic patients as a group had raised SSA (2.65 ± 0.82 mmol l^{-1}, $p = 0.012$) in comparison with normal controls (2.31 ± 0.32 mmol l^{-1}). Sialic acid values were higher than the healthy controls in the 38 normoalbuminuric, 33 microalbuminuric, and 37 proteinuric diabetic patients (2.5 ± 0.66, $2.95 + 1.06$, 2.48 ± 0.68 mmol l^{-1}, respectively) but a significantly higher value was present only in the microalbuminuric group ($p < 0.05$). We did not observe a linear correlation between log SSA and log A/C ratio. No correlation was seen between log SSA and the presence of retinopathy ($n = 40$). SSA values were similar in background, preproliferative and proliferative retinopathy (2.4 ± 0.53 ($n = 20$); 2.4 ± 0.57 ($n = 10$) and 2.7 ± 0.8 mmol l^{-1} ($n = 10$), respectively. Most of the patients with microalbuminuria did not show retinopathic changes. In the controls, there was no effect of gender on SSA values but a significant positive correlation between SSA and systolic BP ($p = 0.023$). However, log transformed SSA in the patients did not show significant correlations with blood pressure, HbA_1 or presence of retinopathy. Multiple linear regression analysis also failed to show an association of SSA with any of these parameters tested in diabetic patients. Only a weak association with BMI was noticed ($p = 0.09$, B = 0.016, SEB = 0.009).

SSA is a marker of acute phase glycoproteins, as it is mainly derived from their metabolism, and may be increased in diabetic patients because of increased concentrations of acute phase proteins found even in the absence of complications.[6–9] Our data contrast with those of Chen *et al*. who found progressive increase in SSA with albuminuria in NIDDM patients.[2] It is likely that in Asian Indians, the acute phase proteins are increased in the diabetic state itself, even in the absence of any specific vascular complications and therefore strong correlation with vascular complications are lacking. It was shown by Pickup *et al*. that Asian Indian Type 2 DM patients without significant coronary heart disease had significantly higher SSA compared to matched group of Caucasians.[5] It is also interesting to note that the mean normal SSA value in the south Indians is higher than the values in Caucasians.

In summary, our study showed that SSA was increased in Indian Asian Type 2 DM patients, maximally in the presence of microalbuminuria. However, in view of the overlap between SSA values in the control and diabetic groups, with and without complications, its use as a specific predictor of diabetic complications is limited.

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